EUROPEAN CHEMICALS AGENCY
BOARD OF APPEAL

DECISION OF THE BOARD OF APPEAL OF THE EUROPEAN CHEMICALS AGENCY

23 August 2022

(Article 42(1) – Follow-up to a compliance check decision – Sections 8.7.2. and 8.7.3. of Annex X – Adaptations from standard information requirements – Section 1.5. of Annex XI – Error of assessment – Proportionality – Animal welfare – Consistency between a compliance check decision and the related follow-up decision – Legitimate expectations – Deadline to provide information after a follow-up decision – Legal certainty)

Case number	A-004-2021
Language of the case	English
Appellant	Celanese Production Germany GmbH & Co. KG, Germany
Representative	Bettina Enderle Environmental Law, Germany
Contested Decision	Decision of 12 January 2021 on the follow-up to a compliance check of a registration for the substance butyl glycollate, adopted by the European Chemicals Agency under Article 42(1) of Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (OJ L 396, 30.12.2006, p. 1; the 'REACH Regulation') The Contested Decision was notified to the Appellant under annotation number CCH-2114538555-43-01/F

THE BOARD OF APPEAL

composed of Antoine Buchet (Chairman), Nikolaos Georgiadis (Technically Qualified Member and Rapporteur), and Marijke Schurmans (Legally Qualified Member)

Registrar: Alen Močilnikar

gives the following

Decision

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1. Background to the dispute

1. This appeal concerns the follow-up to the compliance check of a registration dossier for butyl glycollate (the 'Substance').[1]

2. On 22 October 2010, the Appellant registered the Substance at the tonnage band of 1000 tonnes or more per year.

1.1. The compliance check decision of 14 July 2017

3. On 17 October 2016, the Agency notified to the Appellant a draft compliance check decision in accordance with Articles 41 and 50(1) of the REACH Regulation.[2] In that draft decision, the Agency found that the Appellant's registration dossier had several data-gaps, including under Sections 8.7.2. and 8.7.3. of Annex X.

4. On 23 November 2016, the Appellant submitted comments on the draft compliance check decision in accordance with Article 50(1). The Appellant explained that the data-gaps under Sections 8.7.2. and 8.7.3. of Annex X could be filled with a grouping of substances and read-across adaptation under Section 1.5. of Annex XI. According to the Appellant's adaptation, the Substance is rapidly transformed, once ingested, primarily into same break-down product as would result from the ingestion of an analogue substance, ethylene glycol (the 'Source Substance').[3] It is therefore possible to predict the reproductive and developmental toxicity of the Substance based on existing information on the Source Substance.

5. On 9 March 2017, the Agency notified a revised draft of the compliance check decision to the competent authorities of the Member States in accordance with Articles 50(1) and 51(1). In the revised draft of the compliance check decision, the Agency considered that the adaptation proposed by the Appellant was plausible.

6. On 6 April 2017, the competent authority of Denmark submitted a proposal for amendment to the Agency in accordance with Article 51(2). According to that proposal, the scientific justification for the Appellant's adaptation was insufficient.

7. On 12 May 2017, the Appellant submitted comments on the proposal for amendment in accordance with Article 51(5).

8. On 14 July 2017, following the unanimous agreement of the Member State Committee, the Agency adopted the compliance check decision in accordance with Article 51(6).

9. The compliance check decision of 14 July 2017 stated that the adaptation proposed by the Appellant was plausible but needed to be supported by further information on the metabolism of the Substance, and by evidence that systemic exposure to the non-metabolised Substance is negligible. The Agency therefore found that the Appellant's registration dossier had data-gaps under Sections 8.7.2. and 8.7.3. of Annex X. It consequently required the Appellant to submit, by 21 January 2020:

   - information on a pre-natal developmental toxicity ('PNDT') study in a second species with the Substance (Section 8.7.2. of Annex X), and
   - information on an extended one-generation reproductive toxicity study ('EOGRTS') with the Substance (Section 8.7.3. of Annex X), or
   - alternatively, acceptable adaptations.

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1 EC No 230-991-7, CAS No 7397-62-8.

2 All references to Articles and Annexes concern the REACH Regulation unless stated otherwise.

3 EC No 203-473-3; CAS No 107-21-1.

10. The compliance check decision of 14 July 2017 was not challenged and became final.

1.2. The Appellant's adaptation of 17 January 2020

11. On 17 January 2020, the Appellant submitted a modified version of its adaptation. According to the Appellant's adaptation, information on the Source Substance can be read across to the Substance under Section 1.5. of Annex XI, for Sections 8.7.2. and 8.7.3. of Annex X. Furthermore, the information available on the Source Substance is sufficient to satisfy the information requirements under Sections 8.7.2. and 8.7.3. for the Substance. That information includes, in particular, a PNDT study in a second species (rabbits), and information which is equivalent to an EOGRTS on the basis of a weight-of-evidence approach under Section 1.2. of Annex XI.

12. In support of its adaptation, the Appellant provided, amongst other information, a new *in vitro* enzymatic hydrolysis study – the CRL (2019) study[4] – to investigate the hydrolysis of the Substance in rat liver homogenate, rat small intestinal mucosa homogenate, and rat caecum content.

1.3. The Contested Decision of 12 January 2021

13. On 27 April 2020, the Agency notified to the Appellant a draft follow-up decision in accordance with Articles 42(1) and 50(1). In that draft follow-up decision, the Agency found that the Appellant's adaptation did not comply with the requirements of Section 1.5. of Annex XI.

14. On 2 July 2020, the Appellant submitted comments on the draft follow-up decision in accordance with Article 50(1). The Agency then notified a revised draft to the competent authorities of the Member States in accordance with Articles 50(1) and 51(1).

15. On 12 January 2021, as no competent authority submitted a proposal for amendment, the Agency adopted the Contested Decision in accordance with Article 51(3).

16. In the Contested Decision, the Agency found that the information provided by the Appellant was not sufficient to justify the adaptation under Section 1.5. of Annex XI. In addition, in the Contested Decision, the Agency also found that the information provided by the Appellant was not sufficient to justify an adaptation under Section 1.2. of Annex XI. As a consequence, in the Contested Decision, the Agency:

    - declared that the Appellant's registration dossier still does not comply with the requirements of Sections 8.7.2. and 8.7.3. of Annex XI,
    - declared that the Appellant continues to be required to provide the information required in the compliance check decision of 14 July 2017, and
    - stated that the enforcement authorities of the Member States would be informed of this decision.

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[4] Charles River Laboratories, *In vitro metabolism of butyl glycollate (CAS No. 7397-62-8) in rat liver S9 homogenate, rat small intestinal mucosa homogenate and rat caecum content*, Den Bosch BV, the Netherlands, 2019.

2. Procedure before the Board of Appeal

17. On 9 April 2021, the Appellant filed this appeal.

18. On 11 June 2021, the Agency submitted its Defence.

19. On 6 October 2021, the Appellant submitted observations on the Defence.

20. On 9 November 2021, the Agency submitted its observations on the Appellant's observations on the Defence.

21. On 16 February 2022, a hearing was held as the Board of Appeal considered it necessary. The hearing was held by video-conference in accordance with Article 13(7) of the Rules of Procedure.[5] At the hearing, the Appellant and the Agency made oral submissions and responded to questions from the Board of Appeal.

3. Form of order sought

22. The Appellant requests the Board of Appeal to:

- annul the Contested Decision insofar as it requires the Appellant to submit information on a PNDT study in a second species and an EOGRTS,
- take other or further measures as justice may require, and
- order the refund of the appeal fee.

23. In the event that the appeal should be rejected, the Appellant requests the Board of Appeal to set a new deadline of 36 months, counting from the date on which the decision of the Board of Appeal will become final, for providing information on a PNDT study in a second species and an EOGRTS. In the alternative, the Appellant requests the Board of Appeal to remit the case to the competent body of the Agency for setting such a deadline.

24. The Agency requests the Board of Appeal to dismiss the appeal as unfounded.

4. Assessment of the case

25. The Appellant raises five grounds of appeal, alleging that the Agency:

- committed errors in its assessment of the Appellant's adaptation under Section 1.5. of Annex XI (first ground of appeal),
- breached Sections 1.2. and 1.5. of Annex XI (second ground of appeal),
- breached the principles of legal certainty and of the protection of legitimate expectations (third ground of appeal),
- breached the principle of proportionality (fourth ground of appeal), and
- failed to take account of the provisions of the REACH Regulation concerning the protection of vertebrate animals (fifth ground of appeal).

26. It is appropriate to examine the five grounds of appeal in the order chosen by the Appellant. The fourth and fifth grounds of appeal will be examined together.

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[5] Commission Regulation (EC) No 771/2008 laying down the rules of organisation and procedure of the Board of Appeal of the European Chemicals Agency (OJ L 206, 2.8.2008, p. 5).

4.1. First ground of appeal: Errors in the assessment of the Appellant's adaptation under Section 1.5. of Annex XI

27. By the first ground of appeal, the Appellant argues that the Agency committed several errors in its assessment of its adaptation under Section 1.5. of Annex XI.

28. This ground of appeal consists of seven parts, alleging that the Agency:

- committed an error by not finding that the Substance metabolises rapidly to the same metabolite as the Source Substance (first part),
- applied Section 1.5. of Annex XI incorrectly (second part),
- failed to take into account certain *in vivo* data which are contained or referred to in the Appellant's registration dossier (third part),
- failed to state adequate reasons in the Contested Decision (fourth part),
- made an error of assessment as regards the information provided to satisfy the information requirements for a PNDT study (fifth part),
- made an error of assessment as regards the information provided to satisfy the information requirement for an EOGRTS (sixth part), and
- committed an error by considering that *in vivo* supporting information is necessary for applying Section 1.5. of Annex XI (seventh part).

29. The first, second and third parts of the first ground of appeal will be examined together, as will the fifth and sixth parts.

4.1.1. First, second and third parts of the first ground of appeal: Errors in the assessment of the Appellant's adaptation under Section 1.5. of Annex XI

Arguments of the Parties

30. By the first, second and third parts of the first ground of appeal, the Appellant argues that the Agency committed errors in its assessment of the Appellant's adaptation.

31. First, the Appellant argues that the Agency erred by not finding, in the Contested Decision, that the Substance metabolises rapidly to the same metabolite as the Source Substance. Specifically, according to the Appellant:

- the CRL (2019) study shows that the time required for the amount of the Substance in the blood to be reduced by half (half-life) is 24 minutes *in vitro* in rat liver homogenate, and that all of the Substance is metabolised within 180 minutes of administration,
- a publicly available study on propylene glycol esters – *Domoradzki* et al. (2003)[6] – shows that a half-life of 30 minutes in rat liver homogenate constitutes rapid hydrolysis,
- the *in vivo* hydrolysis of the Substance, following oral administration, is rapid because the Substance is partially or significantly metabolised in the liver, reducing its amount before reaching the systemic circulation (first-pass effect),
- assuming that the Substance is completely absorbed in the intestine after administration does not mean that the entire administered dose contributes to the systemic exposure to the Substance,

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[6] J.Y. Domoradzki *et al*., *Hydrolysis kinetics of propylene glycol monomethyl ether acetate in rats in vivo and in rat and human tissues in vitro*, Toxicological Sciences 75 (2003), pp. 31-39.

- it is irrelevant that the Substance is not metabolised in the small intestines and in the caecum as the rapid metabolism takes place in the liver, and
- several studies and reports – *Klaren et al.* (2019),[7] *Kenyon* et al. (2020),[8] *Domoradzki* et al. (2003), *Lee et al.* (1998),[9] *Bailey and Dickinson* (1999),[10] *Wetmore* (2015),[11] *Wambaugh et al.* (2018),[12] OECD HPV (2003)[13] – show that the rate of hydrolysis of a substance *in vivo* is likely to be more rapid than the rate of hydrolysis measured *in vitro*.

32. Second, the Appellant argues that the Agency applied Section 1.5. of Annex XI incorrectly. According to the Appellant, the Agency committed an error by requiring the Appellant to demonstrate that there is no systemic exposure to the Substance after administration, rather than that there is such a low systemic exposure that the Substance is unlikely to contribute to the overall toxicity.

33. Third, the Appellant argues that the Agency failed to take into account the following *in vivo* data, which are contained or referred to in the Appellant's registration dossier and which show that any non-metabolised amount of the Substance has negligible effects:

- an acute toxicity study on the Substance,
- a 28-day repeated-dose oral toxicity study in rats on the Substance,
- a 90-day repeated-dose oral exposure toxicity study in rats on the Substance,
- a developmental toxicity study in rats on the Substance,
- developmental and reproductive toxicity studies in rats, mice and rabbits on the Substance and the Source Substance.

34. The Agency disputes the Appellant's arguments.

Findings of the Board of Appeal

35. By the first, second and third parts of the first ground of appeal, the Appellant argues that its adaptation complies with the requirements of Section 1.5. of Annex XI. According to the Appellant, the Contested Decision is vitiated by several errors insofar as it rejects that adaptation.

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[7] W.D. Klaren *et al.*, *Identifying attributes that influence in vitro-to-in vivo concordance by comparing in vitro Tox21 bioactivity versus in vivo drug matrix transcriptomic responses across 130 chemicals*, Toxicological Sciences 167/1 (2019), pp. 157 to 171.

[8] E.M. Kenyon *et al*., *Comparison of in vivo derived and scaled in vitro metabolic rate constants for several volatile organic compounds (VOCs)*, Toxicology in Vitro 69 (2020), 105002.

[9] E.A. Lee *et al*., *A method for assaying intestinal brush-border sucrase in an intact intestinal preparation*, Proc. Natl. Acad. Sci. USA, 95 (1998), pp. 2111 to 2116.

[10] M.J. Bailey, R.G. Dickinson, *Limitations of hepatocytes and liver homogenates in modelling in vivo formation of acyl glucuronide-derived drug-protein adducts*, J. Pharmacol. Toxicol. Methods, 41/1 (1999), pp. 27 to 32.

[11] B.A. Wetmore, Qu*antitative in vitro-to-in vivo extrapolation in a high-throughput environment*, Toxicology 332 (2015), pp. 94 to 101.

[12] J.F. Wambaugh *et al*., *Evaluating in vitro-in vivo extrapolation of toxicokinetics*, Toxicological Sciences 163/1 (2018), pp. 152 to 169.

[13] OECD HPV Chemicals Programme, *SIDS Initial Assessment Report for SIAM 17: Propylene Glycol Ethers*, Arona, 11-14 November 2003, av. at https://hpvchemicals.oecd.org/ui/handler.axd?id=fdbb6972-3dd4-4046-ba21-eeb6e28c05fb (last accessed on 19 July 2022).

36. An appeal before the Board of Appeal may only aim to examine whether the evidence submitted by the Appellant is capable of demonstrating that the decision is vitiated by error. In carrying out that examination, the Board of Appeal is not limited to assessing whether the Contested Decision contains errors of assessment which are manifest.[14]

(a) Requirements of Section 1.5. of Annex XI

37. Insofar as is relevant for this case, Section 1.5. of Annex XI provides:

'*Substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as a group, or 'category' of substances. Application of the group concept requires that physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach). This avoids the need to test every substance for every endpoint.*

[…]

The similarities may be based on […] the common precursors and/or the likelihood of common breakdown products via physical and biological processes, which result in structurally similar chemicals.'

38. Section 1.5. of Annex XI therefore allows the registrant of a substance to rely on the information on another substance if it is established that (a) the substances in a group or category are structurally similar, (b) the properties of the substances are likely to be similar or follow a regular pattern, and (c) the similarity of properties or their regular pattern is the result of structural similarity.[15] Those similarities may be based on the likelihood of common breakdown products.

39. The first condition for an adaptation under Section 1.5. of Annex XI is therefore that the source substance(s) and the target substance are structurally similar. This similarity may be based on the likelihood of common breakdown products. Both parties agree that this first condition is fulfilled because the Substance and the Source Substance have a common and relevant metabolite, namely glycolic acid. There is consequently no need to examine the first condition.

40. The second condition for an adaptation under Section 1.5. of Annex XI is that the properties of the source substance(s) and the target substance are likely to be similar or follow a regular pattern. This similarity may also be based on the likelihood of common breakdown products.

41. The Appellant's adaptation is based on the hypothesis that the Substance, once ingested, is broken down rapidly to form the metabolite glycolic acid. This same metabolite is, according to the Appellant's hypothesis, also formed rapidly after the ingestion of the Source Substance. As a consequence, according to the Appellant's hypothesis, the Substance and the Source Substance are likely to have similar properties due to their common break-down product.

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[14] Judgment of 20 September 2019, BASF *Grenzach* v *ECHA*, T-125/17, EU:T:2019:638, paragraphs 81 and 89; see also judgment of 18 November 2020, *Aquind* v *ACER*, T-735/18, EU:T:2020:542, paragraphs 61 and 80.

[15] Decisions of 13 February 2014, *Momentive Specialty Chemicals*, A-006-2012, paragraph 66, and of 23 February 2021, *Lubrizol France and Others*, A-016-2019 to A-029-2019, paragraph 100.

42. According to the Contested Decision, the CRL (2019) study shows that it may take up to 180 minutes for the Substance to be broken down completely. In that time, the Substance may be systemically available within the test organism (systemic exposure) and may cause effects of its own. This is particularly the case in studies involving repeated administration, such as the PNDT study in a second species and the EOGRTS at issue in this case. Therefore, the Contested Decision finds that it is not established that the Substance and the Source Substance are likely to have similar properties due to their common break-down product.

43. In order to determine the merits of the first, second and third parts of the first plea, it is necessary to examine whether the Appellant has shown that the Agency made an error with regard to the second condition for an adaptation under Section 1.5. of Annex XI.

(b) The Agency did not commit an error of assessment by requiring the Appellant to show that systemic exposure to the Substance can be excluded entirely

44. The Appellant argues that the Agency applied Section 1.5. of Annex XI incorrectly by requiring the Appellant to demonstrate that there is no systemic exposure to the Substance after administration, rather than that systemic exposure is so limited that the Substance is unlikely to contribute to overall toxicity.[16]

45. The Contested Decision states in this regard:

'*[The Agency] considers that even though the Substance is eventually (>120 min) converted to the major metabolite glycolic acid […] in the rat liver S9 homogenate a half-life of 24 minutes (liver) indicates that systemic exposure to the unchanged parent substance cannot be excluded. Furthermore, a conversion rate of approximately 20% in the rat intestinal mucosa, and no conversion in the caecum, further indicate potential for the systemic exposure to the unchanged parent compound. Therefore, it is not demonstrated that "repeated oral exposure to the registered substance would lead to such a low systemic exposure that it is unlikely that the parent substance impacts the pre-natal developmental toxicity, i.e. that this toxicity is mediated only via the common metabolite glycolic acid". Therefore, the provided information does not support the rationale for the read-across and you have not demonstrated that the properties of the Substance can be predicted from the properties of the source substance.*

[…]

As explained above [the Agency] noted in the [compliance check decision of 14 July 2017] that in order for the read-across approach to be acceptable, evidence of rapid hydrolysis of the registered substance should be provided, which would confirm that repeated oral exposure to the Substance would lead to such a low systemic exposure to the parent substance that it is unlikely that the parent substance impacts pre-natal developmental toxicity/reproductive toxicity, i.e. that this toxicity is mediated only via the common metabolite glycolic acid […]. ECHA did not require you to demonstrate "no risk".

[…]

Therefore, you have not provided in vitro *or* in vivo *information which would demonstrate that repeated oral exposure to the Substance would lead to low systemic exposure of the parent substance*.'[17]

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[16] Second part of the first ground of appeal, see paragraph 32 above.

[17] Contested Decision, pp. 5 and 6 (emphasis added).

46. Read in isolation, the sentences emphasised in the quotation above, on which the Appellant relies, suggest that the Agency applied Section 1.5. of Annex XI stringently. However, those sentences should not be read in isolation. They must be read in the context of the paragraphs in which they appear in the Contested Decision.

47. It is clear from the quoted part of the Contested Decision, read as a whole, that the Agency did not require the Appellant to show that systemic exposure to the Substance can be excluded entirely. The Agency held that the Appellant's adaptation cannot be accepted because the Appellant has not demonstrated that systemic exposure to the non-metabolised Substance after administration is so low that the Substance is unlikely to produce developmental and/or reproductive effects of its own.

48. That finding is consistent with Section 1.5. of Annex XI, which allows for an adaptation if it is established, *inter alia*, that the properties of the source substance and the target substance are likely to be similar or follow a regular pattern.

49. Therefore, the Agency did not make an error of assessment by requiring the Appellant to show that systemic exposure to the Substance can be excluded entirely.

(c) The Agency did not commit an error in finding that the information provided by the Appellant is not sufficient to show that the Substance metabolises rapidly

50. The Appellant raises seven arguments to show that the Agency committed an error in finding that the Substance has not been shown to metabolise rapidly.[18]

51. First, the Appellant argues that the Agency made an error in finding that the CRL (2019) study does not show that the Substance metabolises rapidly.

52. The CRL (2019) study shows that the Substance has a half-life of 24 minutes *in vitro*. The Substance is expected to be fully metabolised within 180 minutes of each administration.

53. As the Agency explained, based on the findings of the CRL (2019) study the possible toxicological impact of the Substance cannot be assumed to be only due to the common metabolite, and not to the non-metabolised Substance. The CRL (2019) study does not show that the toxicological impact of the non-metabolised Substance as a result of repeated administration does not need to be assessed.

54. Therefore, the Agency did not commit an error in finding that the CRL (2019) study does not demonstrate such rapid metabolisation of the Substance that systemic exposure to the Substance after each administration is negligible.

55. The Appellant's first argument is therefore unfounded.

56. Second, the Appellant argues that the *Domoradzki* et al. (2003) study shows that a half-life of 30 minutes in rat liver homogenate constitutes rapid metabolism.

57. It is not possible to state in the abstract whether a certain half-life is indicative of rapid metabolism or not. That assessment must necessarily be carried out with regard to each specific substance, the available data, and the requirements of Section 1.5. of Annex XI.

[18] First part of the first ground of appeal, see paragraph 31 above.

58. As the Agency explained, the *Domoradzki* et al. (2003) study was not carried out using the Substance. The Appellant has not explained why the findings in that study are relevant to the Substance. Moreover, that study does not take any account of the requirements of Section 1.5. of Annex XI in determining whether a certain rate of metabolism is rapid.

59. Consequently, the fact that in the *Domoradzki* et al. (2003) study a half-life of 30 minutes was said to constitute rapid metabolism for other substances and in a different context does not show that, in the context of the present case, a half-life of 24 minutes means that the Substance is metabolised so rapidly that systemic exposure to the Substance after each administration is negligible.

60. The Appellant's second argument is therefore unfounded.

61. Third, the Appellant argues that there is a first-pass effect in the liver, so that the Substance is metabolised before systemic exposure can take place.

62. It is possible that a significant part of the administered dose is metabolised in the liver directly after ingestion. However, the Appellant provides no evidence to show that this is indeed the case with the Substance, so that only negligible quantities of the Substance are systemically available after each administration. The Appellant's reference to a first-pass effect is an unsubstantiated assertion.

63. The Appellant's third argument is therefore unfounded.

64. Fourth, the Appellant argues that assuming that all the Substance administered to a test animal is completely absorbed through the intestine after administration does not mean that there is systemic exposure to the same amount of the Substance within a test animal after administration.

65. This argument is based on an incorrect reading of the Contested Decision. The Contested Decision refers to the Appellant's statement, made in the decision-making procedure, that in the absence of *in vivo* toxicokinetic studies absorption after administration is by default assumed to be 100%.[19] However, the Contested Decision does not state that this assumption is a reason for finding that the Appellant's adaptation cannot be accepted.

66. As the Agency explained, assuming that the Substance is completely absorbed in the intestine after oral administration does not mean that all of the absorbed Substance will be systemically available. Some, most or even all of the absorbed Substance may be metabolised in the liver after administration.

67. The Appellant has not explained why it considers that the absorption of the Substance after oral administration does not amount to 100%. Moreover, even assuming that the absorption of the Substance after administration were less than 100%, the Appellant has not provided information capable of showing that, whatever quantity of the Substance is absorbed, that quantity is metabolised so rapidly that systemic exposure to the Substance after each administration is negligible.

68. The Appellant's fourth argument is therefore unfounded.

69. Fifth, the Appellant argues that it is irrelevant that the Substance is not metabolised in the small intestines and in the caecum as the metabolism takes place in the liver.

[19] Contested Decision, p. 6.

70. The Contested Decision refers to the fact that the CRL (2019) study shows a conversion rate of approximately 20% in the rat intestinal mucosa, and no conversion in the caecum.[20] As the Agency explained in the course of these appeal proceedings, this means that the Substance, once absorbed, is metabolised elsewhere in the body, presumably in the liver. This does not give any indications as to the rate of metabolism in the liver and does not show that the Substance is metabolised so rapidly that systemic exposure to the Substance after each administration is negligible.

71. The Appellant's fifth argument is therefore unfounded.

72. Sixth, the Appellant argues that several studies and reports – *Klaren et al.* (2019), *Kenyon* et al. (2020), *Domoradzki* et al. (2003), *Lee et al.* (1998), *Bailey and Dickinson* (1999), *Wetmore* (2015), *Wambaugh et al.* (2018), *OECD* (2003) – show that *in vivo* metabolism in the liver is likely to be more rapid than *in vitro* metabolism in liver homogenate.

73. It is possible that the *in vivo* half-life of the Substance may be shorter than the one measured in the CRL (2019) study. However, as the Agency explained, none of the studies and reports to which the Appellant refers addresses the Substance directly. The Appellant has not explained why those studies and reports might be relevant for the Substance.

74. Furthermore, even assuming that the Appellant had shown that those studies and reports are directly relevant for the Substance, those studies and reports, taken together with the CRL (2019) study, would not allow to determine the *in vivo* liver half-life of the Substance. They would merely show that the half-life of the Substance in the liver lies between 2 and 24 minutes after each administration.

75. Consequently, the Agency did not commit an error in concluding that the duration is not so rapid that the non-metabolised Substance will not cause reproductive and/or developmental toxicity effects of its own. The studies and reports to which the Appellant refers are not sufficient to show on their own that the Substance is metabolised so rapidly that systemic exposure to the Substance after each administration is negligible.

76. The Appellant's sixth argument is therefore unfounded.

77. Seventh, the Appellant argues that the Agency failed to take into account *in vivo* data contained or referred to in its registration dossier.

78. The Appellant confined itself to referring to the existence of these studies in its submissions in this case without explaining how they support the Appellant's view that the Substance hydrolyses rapidly.

79. Furthermore, the studies to which the Appellant refers are acute toxicity studies, repeated-dose oral toxicity studies, and reproductive/developmental toxicity studies. These studies are designed to investigate the intrinsic properties of a substance, but not its metabolism or its rate of metabolism.

80. The Appellant's seventh argument is therefore unfounded.

81. It follows that the Appellant has not demonstrated that the Agency committed an error of assessment in finding that the information provided by the Appellant is not sufficient to show that the Substance is metabolised so rapidly that systemic exposure to the Substance after each administration is negligible in this case.

[20] Contested Decision, p. 5.

(d) The Agency did not commit an error by failing to take into account in vivo *information on the reproductive and/or developmental properties of the Substance*

82. The Appellant argues that the Agency failed to take into account certain *in vivo* data which are contained or referred to in the Appellant's registration dossier.[21]

83. It has been found above that the information provided by the Appellant is not sufficient to show that the Substance is metabolised so rapidly that systemic exposure to the Substance after each administration is negligible.[22] Therefore, there may be systemic exposure to the Substance after each administration.

84. On that basis, as the Agency explained, the Appellant's adaptation might be acceptable only if the Appellant could show that although there is systemic exposure to the Substance after each administration, that systemic exposure is not likely to produce reproductive and/or developmental effects of its own.

85. The Appellant refers to an acute toxicity study, a 28-day repeated-dose oral toxicity study in rats on the Substance, a 90-day repeated-dose oral exposure toxicity study in rats on the Substance, a developmental toxicity study on the Substance in rats, and developmental and reproductive toxicity studies on the Source Substance and the metabolite glycolic acid in rats, mice, and rabbits.

86. As regards the acute toxicity study, the 28-day repeated-dose oral toxicity study and the 90-day repeated-dose oral toxicity study, those studies do not investigate the developmental and reproductive effects which are addressed by a PNDT study and by an EOGRTS.

87. As regards the developmental toxicity study on the Substance to which the Appellant refers, that study was carried out in rats and cannot therefore be presumed to provide information on the properties of the Substance which would be addressed by a PNDT study in a second species (rabbits). Moreover, in that type of study the animals are sacrificed before parturition. That type of study therefore does not provide information on the properties of the Substance which would be addressed in an EOGRTS, such as effects on birth, development, growth, and maturation of pups after birth.

88. As regards the remaining developmental and reproductive toxicity studies cited by the Appellant, those studies were carried out on the Source Substance and on the metabolite glycolic acid, not on the Substance. They cannot therefore be presumed to provide information on the Substance unless it is first shown that the requirements for a grouping of substances and read-across adaptation under Section 1.5. of Annex XI are fulfilled.

89. As a consequence, the studies to which the Appellant refers are not capable of showing that systemic exposure to the Substance after each administration is not likely to produce reproductive and/or developmental effects of its own. It follows that the Appellant's reference to the studies in question is not capable of showing that the reproductive and/or developmental effects caused by the possible systemic exposure to the Substance are negligible.

90. It follows that the Agency did not commit an error by failing to take into account *in vivo* information on the reproductive and/or developmental properties of the Substance.

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[21] Third part of the first ground of appeal, see paragraph 33 above.

[22] See paragraphs 50 to 81 above.

(e) Conclusion on the first, second and third parts of the first ground of appeal

91. It follows from the reasons stated above that the Agency did not commit an error by requiring the Appellant to show that the properties of the Substance and the Source Substance are likely to be similar or follow a regular pattern.[23] Furthermore, the Agency did not commit an error in finding that there may be systemic exposure to the Substance,[24] and that the reproductive and/or developmental effects caused by that exposure are unknown.[25]

92. Contrary to the Appellant's arguments, the Agency therefore committed no error in finding, in the Contested Decision, that the second condition for an adaptation under Section 1.5. of Annex XI (likelihood of similar properties or of a regular pattern) is not fulfilled.

93. The Agency was therefore entitled to reject the Appellant's adaptation. As the three conditions of Section 1.5. of Annex XI are cumulative, there was no need for the Agency to examine the third condition.

94. The first, second and third parts of the first ground of appeal are consequently unfounded and must be rejected.

4.1.2. Fourth part of the first ground of appeal: Inadequate statement of reasons

Arguments of the Parties

95. By the fourth part of the first ground of appeal, the Appellant argues that the Contested Decision is not adequately reasoned. First, according to the Appellant, the Agency failed to explain in detail why it considered that the available information does not show that the Substance metabolises rapidly. Second, according to the Appellant, the Contested Decision is inconsistent insofar as it requires the Appellant to show that there is no systemic exposure, rather than low systemic exposure, to the Substance.

96. The Agency disputes the Appellant's arguments.

Findings of the Board of Appeal

97. Under Article 296 of the Treaty on the Functioning of the European Union, Article 41(2)(c) of the Charter of Fundamental Rights, and Article 130 of the REACH Regulation, the Agency must state the reasons for its decisions.

98. The statement of reasons must be appropriate to the act at issue and must disclose in a clear and unequivocal fashion the reasoning followed by the Agency, in such a way as to enable the persons concerned to ascertain the reasons for the measure and to enable the Board of Appeal to exercise its power of review.[26]

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[23] See paragraphs 44 to 49 above.

[24] See paragraphs 50 to 81 above.

[25] See paragraphs 82 to 90 above.

[26] See, to that effect and by analogy, judgment of 21 December 2016, *Club Hotel Loutraki and Others* v *Commission*, C-131/15 P, EU:C:2016:989, paragraph 46; see also decision of 30 January 2018, *Cheminova*, A-005-2016, paragraph 137.

99. In light of the circumstances of a particular case, including its context and all legal rules applicable, it is not necessary for the reasoning in a decision to go into all the relevant facts and points of law, provided that the person concerned can understand the reasons for the decision and the Board of Appeal can exercise its powers of review.[27]

100. Furthermore, the requirements of the duty to state reasons can be attenuated if the measure in question was adopted in circumstances known to the affected person which enable it to understand the scope of the measure.[28] This is the case where a party was closely involved in the process by which the contested decision came about and is therefore aware of the reasons for which the administration adopted it.[29]

101. First, the Appellant argues that the Agency failed to explain in sufficient detail why it considered that the available information does not show that the Substance metabolises rapidly.

102. The Contested Decision states that the CRL (2019) study shows that the Substance has an *in vitro* half-life of 24 minutes in rat liver homogenate, a conversion rate of approximately 20% in the rat intestinal mucosa, and no conversion in the caecum. As a consequence, according to the Contested Decision, it is not established that the Substance is metabolised so rapidly that systemic exposure to the Substance after each administration is negligible.[30] The Contested Decision further addresses and rejects the Appellant's comments concerning the other available information, the absorption rate of the Substance after oral administration, and the possibility that the CRL (2019) study may underestimate the half-life of the Substance.[31]

103. Those explanations are sufficient to allow the Appellant to understand the essential reasons underlying the Agency's position, and to challenge those reasons before the Board of Appeal. They are also sufficient to allow the Board of Appeal to verify whether the Contested Decision is vitiated by error. The Agency consequently complied with the obligation to state reasons in this regard.

104. The Appellant's first argument is consequently unfounded.

105. Second, the Appellant argues that the reasoning in the Contested Decision is inconsistent insofar as it requires the Appellant to show that there is no systemic exposure, rather than low systemic exposure, to the Substance.

106. The duty to state reasons is an essential procedural requirement which must be distinguished from the question whether the reasoning is well founded, which is concerned with the substantive legality of the measure at issue.[32]

107. The Appellant's argument does not concern a formal absence of reasoning, but rather whether the existing reasoning is substantively correct as regards the application of Section 1.5. of Annex XI. Therefore, the Appellant's argument does not show a breach of the duty to state reasons.

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[27] Decision of 13 December 2017, *Akzo Nobel Chemicals and Others*, A-023-2015, paragraph 172.

[28] Judgment of 15 November 2012, *Council* v *Bamba*, C-417/11 P, EU:C:2012:718, paragraph 54.

[29] Judgment of 12 June 1997, *Tiercé Ladbroke* v *Commission*, T-504/93, EU:T:1997:84, paragraph 52; decision of 27 October 2015, *International Flavors & Fragrances*, A-006-2014, paragraph 111.

[30] Contested Decision, p. 5.

[31] Contested Decision, pp. 5 and 6.

[32] Judgment of 14 October 2010, *Deutsche Telekom* v *Commission*, C-280/08 P, EU:C:2010:603, paragraph 130, and decision of 30 January 2018, *Cheminova*, A-005-2016, paragraph 139.

108. In any event, it has already been found that the Agency did not require the Appellant to show that systemic exposure to the Substance can be excluded absolutely. On the contrary, the Agency held that the Appellant's adaptation cannot be accepted because the Appellant has not demonstrated that systemic exposure to the non-metabolised Substance is so low that the Substance is unlikely to produce developmental and/or reproductive effects of its own.[33]

109. The Appellant's second argument is consequently unfounded.

110. The fourth part of the first ground of appeal must therefore be rejected.

4.1.3. Fifth and sixth parts of the first ground of appeal: Errors of assessment as regards the information provided to satisfy the information requirement for a PNDT study on a second species and an EOGRTS

Arguments of the Parties

111. By the fifth part of the first ground of appeal, the Appellant argues that the Agency committed an error of assessment as regards the information provided to satisfy the information requirement for a PNDT study. First, according to the Appellant, the Appellant's adaptation satisfies the requirements of Section 1.5. of Annex XI. Second, according to the Appellant, there is information on a PNDT study in rabbits available on the Source Substance.[34] This study shows an absence of developmental toxicity effects. Third, according to the Appellant, the Contested Decision is incorrect insofar as it states that the information provided by the Appellant is not reliable. According to the Appellant, the study at issue is reliable in that it was carried out correctly, by a reputable test house, and in accordance with good laboratory practice (GLP).

112. By the sixth part of the first ground of appeal, the Appellant argues that the Agency made an error of assessment as regards the information provided to satisfy the information requirement for an EOGRTS. First, according to the Appellant, the Appellant's adaptation satisfies the requirements of Section 1.5. of Annex XI. Second, according to the Appellant, the Contested Decision is incorrect insofar as it states that the information provided by the Appellant is not reliable. Although the Appellant did not provide an EOGRTS on the Source Substance, the available information on the Source Substance and the metabolite glycolic acid is sufficient to predict the properties of the Source Substance which would be investigated in an EOGRTS.

113. The Agency disputes the Appellant's arguments.

Findings of the Board of Appeal

114. As regards the requirement for a PNDT study in a second species under Section 8.7.2. of Annex X, the Appellant provided a PNDT study in rabbits on the Source Substance. As regards the requirement for an EOGRTS under Section 8.7.3. of Annex X, the Appellant provided information on the Source Substance and on the metabolite glycolic acid which – according to the Appellant – is sufficient to predict the properties of the Source Substance which would be investigated in an EOGRTS on the basis of a weight-of-evidence approach.

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[33] See paragraphs 44 to 49 above.

[34] R.W. Tyl *et al*., *Developmental Toxicity Evaluation on Ethylene Glycol by Gavage in New Zealand White Rabbits*, Fundamental and Applied Toxicology 20 (1993), pp. 402-412.

115. The Contested Decision states that the information provided by the Appellant on a PNDT study in rabbits is not reliable, and that the information provided by the Appellant on an EOGRTS is neither reliable nor relevant.[35]

116. It has already been concluded that the Agency made no error in finding that the conditions of Section 1.5. of Annex XI are not fulfilled because there may be systemic exposure to the Substance, and the reproductive and/or developmental effects caused by that exposure are unknown.[36]

117. That reason is in itself sufficient to justify the Agency's rejection of the Appellant's adaptation. It was not necessary for the Agency to examine the information available on the properties of the Source Substance and/or the metabolite glycolic acid. As a consequence, the fifth and sixth parts of the first plea are not capable of leading to the annulment of the Contested Decision.

118. The fifth and sixth parts of the first plea must therefore be rejected as inoperative.

4.1.4. Seventh part of the first ground of appeal: Error of assessment as regards the need for *in vivo* supporting (bridging) studies

Arguments of the Parties

119. By the seventh part of the first ground of appeal, which was raised during the oral hearing, the Appellant argues that the Agency committed an error by considering that information derived from *in vivo* supporting (bridging) studies on the Substance is necessary in this case. According to the Appellant, under the Agency's guidance such information is only required when applying an adaptation under Section 1.5. of Annex XI for substances of unknown or variable composition, complex reaction products or biological materials (UVCB).

120. The Agency disputes the Appellant's argument.

Findings of the Board of Appeal

121. The Contested Decision does not state that the Appellant's adaptation cannot be accepted due to a lack of supporting (bridging) studies. The Contested Decision merely states that the information provided by the Appellant, including the CRL (2019) study, is not sufficient to substantiate the Appellant's adaptation. Therefore, the fact that the Agency argued before the Board of Appeal that further supporting (bridging) studies might have allowed the Appellant to substantiate its adaptation does not show that the Agency committed an error of assessment.

122. The fourth part of the first ground of appeal must therefore be rejected.

4.1.5. Conclusion on the first ground of appeal

123. All seven parts of the first ground of appeal are rejected. The first ground of appeal must consequently also be rejected.

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[35] Contested Decision, pp. 7 to 11.

[36] See section 4.1.1. above.

4.2. Second ground of appeal: Breach of Sections 1.2. and 1.5. of Annex XI

Arguments of the Parties

124. By the second ground of appeal, the Appellant argues that the Agency breached Sections 1.2. and 1.5. of Annex XI for the same reasons as set out under the first ground of appeal.

125. The Agency disputes the Appellant's arguments.

Findings of the Board of Appeal

126. The Contested Decision sets out two separate lines of reasoning as to why the Agency decided to reject the Appellant's adaptation.

127. First, the Contested Decision states that the Appellant's modified adaptation does not satisfy the requirements of Section 1.5. of Annex XI.[37] It has already been found, in the context of the first ground of appeal, that the Agency did not commit an error of assessment in that regard.[38] The second ground of appeal is therefore unfounded insofar as it alleges a breach of Section 1.5. of Annex XI.

128. Second, the Contested Decision states that the Appellant's modified adaptation also does not satisfy the requirements of Section 1.2. of Annex XI.

129. With regard to the requirement for a PNDT study in a second species under Section 8.7.2. of Annex X, the Contested Decision states that although there is a PNDT study in rabbits on the Source Substance, that study cannot be used to satisfy the information requirements for the registration of the Substance because the requirements of Section 1.5. of Annex XI are not fulfilled.[39]

130. With regard to the requirement for an EOGRTS under Section 8.7.3. of Annex X, the Contested Decision states that:

- the Appellant did not provide an EOGRTS study on either the Substance or the Source Substance, but instead sought to rely on other studies on the Source Substance and the metabolite glycolic acid in a weight-of-evidence approach;
- those studies cannot be used to satisfy the information requirements for the registration of the Substance because the requirements of Section 1.5. of Annex XI are not fulfilled; and
- in any event, those studies are not sufficient to provide, even on the Source Substance, the information that would otherwise be obtained from an EOGRTS.[40]

131. The Agency made no error in finding that the conditions of Section 1.5. of Annex XI are not fulfilled.[41] As a consequence, the Appellant could not rely on the information on the Source Substance and/or the metabolite glycolic acid for the purpose of registering the Substance. Therefore, it was not necessary for the Agency to examine the information available on the properties of the Source Substance and/or the metabolite glycolic acid.

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[37] Contested Decision, pp. 3 to 6.

[38] See section 4.1. above.

[39] Contested Decision, pp. 7 to 9.

[40] Contested Decision, pp. 9 to 11.

[41] See section 4.1. above.

132. The second ground of appeal is therefore inoperative insofar as it alleges a breach of Section 1.2. of Annex XI.

133. The second ground of appeal must consequently be rejected.

4.3. Third ground of appeal: Breach of the principles of legal certainty and of the protection of legitimate expectations

134. By the third ground of appeal, the Appellant argues that the Agency breached the principles of legal certainty and of the protection of legitimate expectations. This ground of appeal consists of two parts.

4.3.1. First part of the third ground of appeal: Inconsistency between the compliance check decision of 14 July 2017 and the Contested Decision

Arguments of the Parties

135. By the first part of the third ground of appeal, the Appellant argues that the compliance check decision of 14 July 2017 and the Contested Decision contradict each other. According to the Appellant, the compliance check decision of 14 July 2017 stated that an adaptation under Section 1.5. of Annex XI for the Substance is plausible, provided that the Appellant could show that there is low systemic exposure to the Substance. In the Contested Decision, however, the Agency held that the Appellant has not shown that systemic exposure to the Substance can be excluded.

136. The Agency disputes the Appellant's arguments.

Findings of the Board of Appeal

137. The principle of legal certainty requires that rules of law must be clear and precise, and that their application must be foreseeable by those subject to them.[42]

138. The principle of the protection of legitimate expectations is a corollary of the principle of legal certainty.[43] It presupposes that the administration gave the person concerned precise assurances, leading that person to entertain justified expectations. Information which is precise, unconditional and consistent, in whatever form it is given, constitutes such assurances.[44]

139. In the present case, the compliance check decision of 14 July 2017 stated that the adaptation proposed in the Appellant's comments on the draft decision was plausible with regard to the requirements for a PNDT study and an EOGRTS, but needed to be supported by further evidence:

> *'[I]n order for the read-across approach to be acceptable, evidence of […] the rapid hydrolysis of the registered substances by esterases should be provided, which would confirm your claim that repeated oral exposure to the registered substance would lead to such low systemic exposure that it is unlikely that the parent substance impacts the pre-natal developmental toxicity, i.e. that this toxicity is mediated only via the common metabolite glycolic acid […].*

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[42] Judgment of 11 September 2019, *Călin*, C-676/17, EU:C:2019:700, paragraph 50.

[43] Judgment of 3 December 2019, *Czech Republic* v *Parliament and Council*, C-482/17, EU:C:2019:1035, paragraph 153.

[44] Judgment of 16 September 2021, *FVE Holýšov I and Others* v *Commission*, C-850/19 P, EU:C:2021:740, paragraph 34.

[The Agency] considers that the read-across should be further strengthened by additional evidence with the registered substance, e.g. toxicokinetic (hydrolysis/metabolism) information and/or modelling, to address the shortcomings described above.'[45]

140. The Appellant provided a modified justification for its adaptation, including the CRL (2019) study, by the relevant deadline.[46] In the Contested Decision, the Agency then found that the information provided by the Appellant was not sufficient to satisfy the requirements of Section 1.5. of Annex XI:

'*[The Agency] considers that even though the Substance is eventually (>120 min) converted to the major metabolite glycolic acid […] in the rat liver S9 homogenate, a half-life of 24 minutes (liver) indicates that systemic exposure to the unchanged parent compound cannot be excluded. Furthermore, a conversion rate of approximately 20% in the rat intestinal mucosa, and no conversion in the caecum, further indicate potential for the systemic exposure to the unchanged parent compound. Therefore, it is not demonstrated that* "repeated oral exposure to the registered substance would lead to such a low systemic exposure that it is unlikely that the parent substance impacts the pre-natal developmental toxicity, i.e. that this toxicity is mediated only via the common metabolite glycolic acid*". Therefore, the provided information does not support the rationale for the read-across and you have not demonstrated that the properties of the Substance can be predicted from the properties of the source substance.'*[47]

141. It is therefore clear that the Agency considered, in both decisions, that an adaptation under Section 1.5. of Annex XI could be accepted if several conditions are met. In particular, the adaptation might be acceptable if the Appellant could show that repeated oral exposure to the Substance leads to such low systemic exposure to the (non-metabolised) Substance that is likely not to have toxicological effects of its own. The Agency did not state that the Appellant's adaptation would certainly be accepted if the Appellant carried out an *in vitro* hydrolysis study, such as the CRL (2019) study.

142. Therefore, contrary to the Appellant's argument, there is no inconsistency in this regard between the compliance check decision of 14 July 2017 and the Contested Decision.

143. The first part of the third ground of appeal is therefore unfounded.

4.3.2. Second part of the third ground of appeal: Extension of the time-limit set in the compliance check decision of 14 July 2017

Arguments of the Parties

144. By the second part of the third ground of appeal, the Appellant argues that the Agency should have set a time-limit, in the Contested Decision, for the Appellant to provide information on a PNDT study second species and an EOGRTS on the Substance, or alternatively an acceptable adaptation.

145. According to the Appellant, the Contested Decision should have extended the time-limit set in the compliance check decision of 14 July 2017. Failing to extend that time-limit constitutes a breach of the principle of legal certainty.

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[45] Compliance check decision of 14 July 2017, pp. 5, 8 and 9.

[46] See paragraphs 11 and 12 above.

[47] Contested Decision, p. 5.

146. Furthermore, according to the Appellant, the present case differs from the case that led to the decision of the Board of Appeal of 21 October 2020, *Solvay Fluor*, A-001-2019, as the Appellant does not seek a new time-limit, but a prolongation of the time-limit set in the compliance check decision of 14 July 2017.

147. The Agency disputes the Appellant's arguments.

Findings of the Board of Appeal

148. The time-limit set in the compliance check decision of 14 July 2017 expired on 21 January 2021, which was before the adoption of the Contested Decision. As a consequence, the Agency could not extend that time-limit in the Contested Decision. The Appellant's argument therefore means, in effect, that the Agency should have set a new time-limit in the Contested Decision. In this respect, the present case is identical to *Solvay Fluor*.

149. In *Solvay Fluor*, the Board of Appeal found that a follow-up decision under Article 42(1) – such as the Contested Decision – does not require from a registrant any information other than the information already identified in the compliance check decision under Article 41. A follow-up decision under Article 42(1) is strictly limited to assessing whether the data-gaps identified in the initial compliance check decision have been filled. Article 42(1) does not oblige the Agency to set a new deadline.[48]

150. Furthermore, the absence of a new deadline in the Contested Decision is consistent with the principle of legal certainty. The possibility that an adaptation may be rejected, and that enforcement measures might ensue following a decision under Article 42(1), is foreseeable to a registrant when it decides whether to submit an adaptation or carry out a study in consequence of a compliance check decision.[49]

151. Therefore, contrary to the Appellant's arguments, the Agency could not extend the time-limit set in the compliance check decision of 14 July 2017 and was not required to set a new time-limit.

152. The second part of the third ground of appeal is therefore unfounded.

4.3.3. Conclusion on the third ground of appeal

153. As both parts of the third ground of appeal are unfounded, that ground of appeal must be rejected.

4.4. Fourth and fifth grounds of appeal: Breaches of the principle of proportionality and of the principle that testing on vertebrate animals should be carried out only as a last resort

Arguments of the Parties

154. By the fourth ground of appeal, the Appellant argues that the requirement to provide information on a PNDT study in a second species and on an EOGRTS on the Substance is disproportionate. Specifically, the Appellant argues that:

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[48] Decisions of 21 October 2020, *Solvay Fluor*, A-001-2019, paragraphs 43 to 75, and of 9 November 2021, *Polynt*, A-009-2020, paragraphs 44 to 48, currently challenged before the General Court.

[49] See, by analogy, judgment of 23 January 2019, *Deza* v *ECHA*, C-419/17 P, EU:C:2019:52, paragraph 71; see also judgment of 21 January 2021, *Germany* v *Esso Raffinage*, C-471/18 P, EU:C:2021:48, paragraphs 140 and 141.

- the Appellant has provided information in support of its adaptation – such as the CRL (2019) study – which shows that the metabolite glycolic acid drives the toxicity of both the Substance and the Source Substance;
- the required information on a PNDT study in a second species and on an EOGRTS is unlikely to provide meaningful results because the results are likely to be equivalent to the results obtained in the studies carried out on the Source Substance and the metabolite glycolic acid; the Appellant relies, in this regard, on paragraphs 200 and 201 of the decision of the Board of Appeal of 29 April 2013, *Honeywell Belgium*, A-005-2011; and
- providing information on a PNDT study in a second species and on an EOGRTS requires the sacrifice of numerous animals and considerable expenditure, whilst it is unlikely that this information will achieve a higher level of protection of human health.

155. By the fifth ground of appeal, the Appellant argues that the requirement to provide information on a PNDT study in a second species and on an EOGRTS on the Substance is contrary to the principle that testing on vertebrate animals should be carried out only as a last resort.

156. The Agency disputes the Appellant's arguments.

Findings of the Board of Appeal

157. The Appellant argues that it is disproportionate and contrary to Articles 25(1) and 13(1) to carry out a PNDT study in a second species and an EOGRTS on the Substance, as similar studies are available on the Source Substance.

158. As concluded above, the Agency made no error in finding that the Appellant's adaptation did not comply with the requirements of Section 1.5. of Annex XI. Therefore, the Appellant cannot rely on studies on the Source Substance for the purposes of its registration of the Substance. This is in line with Articles 25 and 13(1). The Appellant's registration for the Substance consequently continues to have data-gaps under Column 1 of Sections 8.7.2. and 8.7.3. of Annex X.[50]

159. The consequences of that finding flow directly from Article 10(a)(vi) and (vii) and Article 12, read in conjunction with the standard information requirements in Column 1 of Sections 8.7.2. and 8.7.3. of Annex X. Under those provisions, the Appellant remains obliged to provide information on the relevant studies, or acceptable adaptations. [51]

160. As no acceptable adaptation has been provided, the Agency was neither required nor empowered to consider whether it is consistent with the principle of proportionality for the Appellant to continue to be required to submit information on the relevant studies, or acceptable adaptations.[52] For the same reason, the Agency also did not contravene the principle that animal studies should be carried out only as a last resort, which is set out in Articles 25 and 13(1).[53]

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[50] See section 4.1. above.

[51] Decision of 11 December 2018, *Climax Molybdenum*, A-006-2017, paragraph 121.

[52] See, by analogy, decision of 4 May 2018, *Clariant Plastics & Coatings (Deutschland)*, A-011-2018, paragraph 51; see also judgment of 16 March 2022, *MEKH* v *ACER*, T-684/19, EU:T:2022:138, paragraphs 50 and 51.

[53] See, by analogy, decision of 4 May 2018, *Clariant Plastics & Coatings (Deutschland)*, A-011-2018, paragraph 51.

161. That conclusion is not called into question by the Appellant's reference to *Honeywell Belgium*, to which the Appellant refers.[54] That case concerned Column 2 of Section 8.6.4 of Annex X, which gives the Agency discretion to decide whether further information on a substance is necessary, and which information this should be. The present case, by contrast, concerns Column 1 of Sections 8.7.2. and 8.7.3. of Annex X, which are standard information requirements for which the Appellant failed to provide an acceptable adaptation, and therefore give the Agency no discretion in that regard. *Honeywell Belgium* therefore differs from the present case in a fundamental respect.

162. The fourth and fifth grounds of appeal must therefore be rejected.

4.5. Result

163. As all the grounds of appeal have been rejected, the appeal must be dismissed.

5. Request for the setting of a deadline

164. In the event that the Appeal is dismissed, the Appellant requests the Board of Appeal to set a deadline of 36 months for the Appellant to provide information on a PNDT study in a second species and on an EOGRTS, or to remit the case to the competent body of the Agency for such a deadline to be set. The Appellant justifies this request by reference to its arguments on the requirements of the principle of legal certainty.[55]

165. Under Article 93(3), following its examination of a case, the Board of Appeal may exercise any power that lies within the competence of the Agency or remit the case to the competent body of the Agency for further action.

166. That provision governs solely the powers of the Board of Appeal after having held that an action before it was well founded. If an appeal is unfounded, the Board of Appeal has no power to alter the operative part of a contested decision.[56]

167. In the present case, the appeal has already been held to be unfounded. In particular, the Appellant's argument that the Contested Decision should have set a deadline for the provision of information on a PNDT study in a second species and an EOGRTS has been rejected for the reasons set out in section 4.3.2. above.

168. The request for the setting of a deadline must therefore be rejected.

6. Refund of the appeal fee

169. Under Article 10(4) of the Fee Regulation,[57] the appeal fee must be refunded if the appeal is decided in favour of an appellant. As the appeal is dismissed, the appeal fee is not refunded.

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[54] See paragraph 154 above.

[55] See paragraphs 144 to 146 above.

[56] Judgment of 20 September 2019, *BASF Grenzach* v *ECHA*, T-125/17, EU:T:2019:638, paragraphs 66 and 118; decisions of 22 June 2021, *Tecnofluid*, A-002-2020, paragraph 58, and of 5 February 2020, *Sustainability Support Service (Europe)*, A-022-2018, paragraph 20.

[57] Commission Regulation (EC) No 340/2008 on the fees and charges payable to the European Chemicals Agency pursuant to the REACH Regulation (OJ L 107, 17.4.2008, p. 6).

On those grounds,

THE BOARD OF APPEAL

hereby:

1. **Dismisses the appeal.**
2. **Rejects the request for the setting of a deadline to provide the information required by the compliance check decision of 14 July 2017.**
3. **Decides that the appeal fee is not refunded.**

Antoine BUCHET
Chairman of the Board of Appeal

Alen MOČILNIKAR
Registrar of the Board of Appeal